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10/698,402	11/03/2003	Jean-Louis Escary	60711.000025	2689

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EXAMINER	
SEHARASEYON, JEGATHEESAN	

ART UNIT	PAPER NUMBER
1647	

DATE MAILED: 06/26/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/698,402	ESCARY, JEAN-LOUIS	
	Examiner	Art Unit	
	Jegatheesan Seharaseyon, Ph.D	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 March 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-62* is/are pending in the application.

4a) Of the above claim(s) *1-38,48,51,52 and 54-56* is/are withdrawn from consideration.

5)☐ Claim(s) *53,57-59 and 61* is/are allowed.

6)☒ Claim(s) *39,42,45,49,50,60 and 62* is/are rejected.

7)☒ Claim(s) *40,41,43,44,46 and 47* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. This office action is in response to the amendment and remarks filed on 3/29/06. Claims 57-62 have been added. Claims 32, 33, 35,39-50 and 53 have been amended. Therefore, claims 1-62 are currently pending. Claims 1-38, 48, 51, 52 and 54-56 are withdrawn. Claims 39-47, 49, 50, 53 and 57-62 are examined.

2. The change of title is acknowledged.

3. Receipt of the certified copy of the priority document is acknowledged.

4. Receipt of the copies of the Oath/Declaration is acknowledged.

5. The text of those sections of Title 35, U. S. Code not included in this action can be found in a prior Office action.

6. Any objection or rejection of record, which is not expressly repeated in this action, has been overcome by Applicant's response and withdrawn.

7. Claims 53, 57-59 and 61 are directed to an allowable product. Pursuant to the procedures set forth in MPEP § 821.04(b), claims 49 and 50, directed to the process of making or using the allowable product, previously withdrawn from consideration as a result of a restriction requirement, is hereby rejoined and fully examined for patentability under 37 CFR 1.104. Claims 1-35, 36-38, 48, 51-52 and 54-56, directed to the invention(s) of 1-2, 4 and 6 do not require all the limitations of an allowable product claim, and are NOT been rejoined.

Because a claimed invention previously withdrawn from consideration under 37 CFR 1.142 has been rejoined, **the restriction requirement between groups 3 and 5 as set forth in the Office action mailed on 6/21/2005 is hereby withdrawn.** In view

of the withdrawal of the restriction requirement as to the rejoined inventions, applicant(s) are advised that if any claims including all the limitations of an allowable product claim or rejoined process claim are presented in a continuation or divisional application, such claims may be subject to provisional statutory and/or nonstatutory double patenting rejections over the claims of the instant application. Once the restriction requirement is withdrawn, the provisions of 35 U.S.C. 121 are no longer applicable. See *In re Ziegler*, 443 F.2d 1211, 1215, 170 USPQ 129, 131-32 (CCPA 1971). See also MPEP § 804.01.

Claim Objections

8. Claims 40, 41, 43, 44, 46, 47 are objected as depended on rejected claims.

Claim Rejections - 35 USC § 112, maintained

9. The rejection of claims 39, 42 and 45 under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention is maintained for reasons set forth in the Office Action dated 12/19/2005. This rejection is also applied to newly added claims 60 and 62.

Applicant's arguments have been fully considered but are not found to be persuasive. Applicant asserts that despite some differences their amino acid sequences, all of the polypeptides belonging to the IFNα family share a common structure and common anti-proliferative, antiviral and immunomodulatory function. Further it is asserted that there is 80% homology between the IFNα proteins with

common function (see page 15, first paragraph of the response). Therefore, it is asserted that the inventor was in possession of the genus of polypeptide instantly claimed. This argument is not found to be persuasive because even though, the overall comparison is given for the various IFNαs, the specification does not provide teachings for the regions or domain needed for the specific activities or specific changes in the IFNα5 polypeptide (up to 90% identity) and yet retain the anti-viral or anti-tumoral activities. A polypeptide, which has 90% identity to SEQ ID NO: 2, requires that there be around 19 amino acid changes in the polypeptide (IFNα5 is 189 amino acid long). However, the specification fails to disclose a polypeptide that contains up to 19 amino acid changes and yet retain either anti tumor or anti viral activities of the instant polypeptide. Furthermore, the specification and the claims do not disclose the identification of any particular portion of the IFNα5 structure that must be conserved in order to conserve the required function. Therefore, the rejection of record is maintained with respect to polypeptides containing 90% sequence identity to SEQ ID NO:2.

9. The rejection of claims 39, 42 and 45 under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an interferon-α5 variant up to 95% sequence identity, with substitutions such as C122S of SEQ ID NO: 2 of the wild type protein which has antiviral activity (see Figure 3 of the specification), the disclosure does not reasonably provide enablement for all variants of interferon-α5 (up to 90%) contemplated and which anti-viral or anti-tumoral activities. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly

connected, to make and use the invention commensurate in scope with these claims. This rejection is also applied to newly added claims 60 and 62.

Applicant asserts that they have provided sufficient disclosure on how to make and use a genus of interferon-α5 polypeptides which share at least 90% sequence homology with SEQ ID NO: 2 wherein said polypeptides comprise a Q28R, Q70E or C122S, and which retain interferon-α5 activities (see pages 15-17 of the response). It is asserted that there is 80% homology between the IFNα proteins with common function (see page 16, second paragraph of the response). Therefore, it is asserted that the inventors are enabled for the genus of polypeptide instantly claimed. This argument is not found to be persuasive because even though, the overall comparison is given for the various IFNαs, the specification does not provide enabling disclosure for the specific changes in the IFNα5 polypeptide and yet retain the anti-viral or anti-tumoral activities. A polypeptide, which has 90% identity, requires that there be around 19 amino acid changes in the polypeptide (IFNα5 is 189 amino acid long). However, the specification fails to disclose a polypeptide that contains up to 19 amino acid changes and retain either anti tumor or anti viral activities of the instant polypeptide.

While Hu et al. reference discloses changes at positions 86 and 90 of IFNα, it fails to teach changes leading to a 90% variant which retains the anti-viral and anti-tumoral activity of IFN-α5. Despite knowledge in the art for producing variants of a given polypeptide with amino acid deletions, insertions or substitutions the specification fails to provide any guidance regarding the changes/modifications contemplated and yet retain the function(s) of the interferon-α5 variants claimed. The Applicant has provided

little or no guidance beyond the mere presentation of sequence data to enable one of ordinary skill in the art to determine, without undue experimentation, the positions in the protein which are tolerant to change (e.g. such as by amino acid substitutions or deletions), and the nature and extent of changes that can be made in these positions. Although the specification outlines art-recognized procedures for producing and screening for active variants, this is not adequate guidance as to the nature of active derivatives that may be constructed, but is merely an invitation to the artisan to use the current invention as a starting point for further experimentation. Undue amount of experimentation would be required to generate changes/modifications contemplated and yet retain the function of the proteins claimed.

Applicant has not taught how one of skill in the art would use the full scope of polypeptide sequences encompassed by the invention of claims 39, 42 and 45. The specification as filed does not sufficiently teach one of skill in the art how to make and/or use the full scope of the claimed sequences. The amount of experimentation required to make and/or use the full scope of the claimed sequences would require trial and error experimentation to determine the functional sequences. Given the breadth of claims 39, 42 and 45 in light of the unpredictability of the art as determined by the lack of working examples and shown by the prior at of record, the level of skill of the artisan, and the lack of guidance provided in the instant specification, it would require undue experimentation for one of ordinary skill in the art to make and use the claimed invention.

Claim Rejections - 35 USC § 112, first paragraph (new)

10. Claim 49 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Claim 49 is drawn to treating or preventing a disease or disorder linked to interferon alpha-5 by administering a polypeptide of SEQ ID NO: 2. Applicants have evaluated the anti-viral and anti-tumoral activity of the interferon alpha-5 polypeptide comprising the C122S mutation (pages 55-57). However, the specification as filed is insufficient to enable one of skilled in the art to practice the claimed invention of treating or preventing a disease or disorder linked to interferon alpha-5 without an undue amount of experimentation because the specification and the prior art have not established the interferon alpha-5 linked disorders. Thus the pathology of a disease or disorder linked to interferon alpha-5 are not known. For example, CFTR gene is linked to cystic fibrosis and Duchene Muscular Dystrophy gene is linked to DMD. Even if a disease or disorder linked to interferon alpha-5 are known it is not clear if it can be prevented.

If one skilled in the art is not guided as to the pathology of the a disease or disorder linked to interferon alpha-5, then the skilled artisan is also not guided as to how to use methods for the treatment or prevention using the compositions comprising these polypeptides. Since, there is inadequate guidance as to the nature of the invention, it is merely an invitation to the artisan to use the current invention as a starting point for

further experimentation to try various disease or disorder linked to interferon alpha-5 for prevention and treatment. In addition, because there is no working examples provided describing diseases or models it would require an undue amount of experimentation to one of skill in the art to practice the claimed invention. In addition, there is no mechanism associated with a disease or disorder linked to interferon alpha-5 recited in the claims. While mechanism is not required, it can allow extrapolation of enablement to non-exemplified embodiments.

Given the breadth of claim 49 in light of the unpredictability of the art as determined by the lack of working examples, the level of skill of the artisan, and the lack of guidance provided in the instant specification and the prior art of record, it would require undue experimentation for one of ordinary skill in the art to make and use the claimed invention for a method of treatment or method of preventing a disease or disorder linked to interferon alpha-5 by administering interferon alpha-5 polypeptides.

11. Claim 50 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while enabling for treating (antiviral activity against vesicular stomatitis virus (VSV) *in vitro*, Encephalomyocarditis virus (EMCV) *in vivo* (mouse model) and anti-tumoral activity against Friend erythro leukemia cells (FLC) injected mice, does not reasonably provide enablement for the treatment or prevention of cancers, tumors and immunological diseases. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Claim 50 is drawn to treating or preventing cancers, tumors and immunological diseases by administering a polypeptide of SEQ ID NO: 2. Applicants have evaluated the antiviral and antiproliferative activity of the interferon alpha-5 polypeptide comprising the C122S mutation (pages 55-57). Specifically, Applicants demonstrate antiviral activity against vesicular stomatitis virus (VSV) *in vitro*, against Encephalomyocarditis virus (EMCV) *in vivo* and anti-tumoral activity against Friend erythro leukemia cells (FLC) injected mice. However, the specification as filed is insufficient to enable one of skilled in the art to practice the claimed invention of treating or preventing all cancers, tumors and immunological diseases without an undue amount of experimentation because the specification and the prior art have not treated or prevented all viral diseases.

Applicant has not disclosed how to use the claimed invention to treat or prevent all cancers, tumors and immunological diseases of the subjects. There is insufficient evidence of the invention with respect to the *in vivo* operability of the claimed invention. In addition, there is no guidance provided in choosing the treatment regimen with therapeutically effective amount for administering to the subjects. Pharmaceutical therapies are unpredictable for the following reasons; (1) the proteins may be inactivated before producing an effect, i.e. such as proteolytic degradation, immunological inactivation or due to an inherently short half life protein; (2) the protein may otherwise not reach the target area because, for example, the protein may not be able to cross the mucosa; (3) other functional properties, known or unknown, may make the protein unsuitable for *in vivo use*, i.e. may produce adverse side effects prohibitive to the using of such treatment.

Since, there is inadequate guidance as to the nature of the invention, it is merely an invitation to the artisan to use the current invention as a starting point for further experimentation for preventing or treating all cancers, tumors and immunological diseases by administering the polypeptide of the instant invention. In addition, because there are only two *in vivo* working examples provided describing diseases or models it would require an undue amount of experimentation to one of skill in the art to practice the claimed invention.

Given the breadth of claim 50 in light of the unpredictability of the art as determined by the lack of working examples, the level of skill of the artisan, and the lack of guidance provided in the instant specification and the prior art of record, it would require undue experimentation for one of ordinary skill in the art to make and use the claimed invention for a method of treatment or method of preventing all viral diseases by administering interferon alpha-5 polypeptides.

12. Claims 53, 57-59 and 61 are allowable. In addition, if claims 40, 41, 43, 44, 46 and 47 are written as independent claims they will be allowable.

13. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any

extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Contact Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jegatheesan Seharaseyon, Ph.D whose telephone number is 571-272-0892. The examiner can normally be reached on M-F: 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brenda Brumback can be reached on 571-272-0961. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

JS 06/06

CHRISTINE J. SAOUD
PRIMARY EXAMINER

Christine J. Saoud